REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the claims

No claims are newly amended, added, cancelled or withdrawn, and are presented solely for the convenience of prosecution. Pending are claims 1, 2, 4, 5, 7-14, 16-21 and 24-29. Claims 3, 6, 15, 22 and 23 were previously cancelled. Claims 2, 8-14, 16-21, and 24-29 are withdrawn. Claims 1, 4, 5 and 7 are under examination Applicant respectfully requests entry and consideration of the withdrawn subject matter upon the identification of allowable subject matter in the generic or linking claims.

II. Rejection under 35 U.S.C. § 103

The present invention is directed to the combined use of (1) an acidifying agent and (2) a cationic surfactant for pretreatment of a sample for the purpose of the release of HCV antigen and the inactivation of antibodies that bind to the HCV antigen.

Pages 3-7 of the Action maintains the rejection of claims 1, 4, 5 and 7 as allegedly obvious over the combination of WO 00/07023 to Aoyagi, as found in U.S. Patent No. 7,316,915 (Aoyagi III), in combination with Aoyagi II (WO 99/06836, equivalent to EP 0 967 484 (EP '484) and U.S. Application No. 09/269,897, hereinafter "US 09/269897"). The Advisory Action complains that the Tables do not provide a comparison to the closest prior art to support assertions of unexpected results. Applicant respectfully traverses the rejection, for reasons of record, and in view of the following remarks which also provide the comparisons that are requested by the Examiner.

The Office acknowledges that Aoyagi III does not teach or suggest the use of an acidifying agent (Action at page 4, first full paragraph) for pretreatment, but alleges that this defect is remedied by US 09/269897. US 09/269897 discloses a combined use of (1) an anionic surfactant and (2) amphoteric surfactant, nonionic surfactant or protein decomposing agent for pretreatment of a sample for the purpose of releasing antigen. Because an acid is listed as a protein decomposing agent, US 09/269897 may be considered to describe the

combined use of an anionic surfactant and an acidifying agent. US 09/269897 does not describe the use of a cationic surfactant in the pretreatment. Therefore, the presently claimed pretreatment with a ***cationic surfactant*** and acidifying agent differs from US 09/269897's disclosure of pretreatment with an ***anionic surfactant*** and an acidifying agent.

The only disclosure of a cationic surfactant in US 09/269897 is found in Example 15. This, however, describes the use of a cationic surfactant in a reaction mixture for ***assaying*** antigen, and is not in the ***pretreatment*** step for releasing the antigen. *See, e.g.* US 09/269897, page 55, line 32, to page 56, line 3. Therefore, US 09/269897 teaches the use of the cationic surfactant at a completely different step in the assay, for a different purpose, to that presently claimed.

The use of a cationic surfactant instead of anionic surfactant in the pretreatment step provides an unexpected advantage that is not explained merely by the remaining presence of cationic surfactant in the subsequent assay for HCV proteins. That is, the ***order*** in which a cationic surfactant is used is important. The benefit of a cationic surfactant in the pretreatment step may be demonstrated by comparing Tables 1 and 2 of the present invention and Table 10 of US 09/269897. These tables report on the assay results (i.e., after pretreatment), which are expressed as reactivity relative to normal human serum.

The effect of a concentration of surfactant in the assay may be compared by examining amount of antigen detected in the presence of the surfactant, adjusted for results in the absence of surfactant. Both the present application and US 09/269897 describe results with 0% surfactant (i.e. without addition) and 0.5%, permitting a comparison between the two disclosures. To calculate the effect provided by the addition of 0.5% cationic surfactant, a ratio is calculated in comparison with the non-addition (0%) (the background). This may be referred to as an "S/N ratio." A summary of these derived data is shown in the enclosed **Table A**.

Regarding cationic surfactants having 10 carbon atoms, decyltrimethylammonium chloride, also known as n-decyltrimethylammonium chloride, is common to both the present application and US 09/269897. For the present invention the average 0.5%/0% S/N ratio of

the samples #10, #120, #117 and #89 is **2.65**. On the other hand, for US 09/269897, the average 0.5%/0% S/N ratio of the samples #45, #3, #7 and #19 is **0.775**. Therefore, a far better relative sensitivity (S/N ratio) is obtained by the addition of Decyltrimethylammonium chloride into a pretreatment solution (2.65) in comparison with the addition of the same surfactant into an assay solution according to US 09/269897 (0.775).

In addition, regarding sample #89, as can be seen from Tables 1 and 2, the baseline (no surfactant) value is abnormally high, 0.322, in comparison with the corresponding values of other samples (for example, 0.123 for #117). This may be due to the samples being pretreated with 0.5N HCl, and therefore, the baseline value may be apparently be higher than normal value. Considering the result for #89 in Fig. 1, in which the baseline value at 0.0 N HCl is about 0.1 and that at 0.5N HCl is about 0.3, it appears that the baseline for #89 in Tables 1 and 2 "0.322" is too high by about 0.2. Therefore, the baseline value for #89 should be correctly about "0.2." According to re-calculation considering the above, for the present invention an average 0.5%/0% S/N ratio of the samples #10, #120, #117 and #89 is **3.525** which is even higher that **0.77** of US 09/269897.

Regarding cationic surfactants having 12 carbon atoms, lauryl pyrimidium chloride, also known as dodecyl pyrimidium chloride, is common to both the present invention and US 09/269897. According to the same calculation as explained above for cationic surfactant having 10 carbon atoms, for the present invention an average 0.5%/0% S/N ratio of the samples #10, #120, #117 and #89 is **2.8**, or **3.475** if correcting for the aberrant baseline in #89. On the other hand, for US 09/269897, an average 0.5%/0% S/N ratio of the samples #45, #3, #7 and #19 is **2.60**. Therefore, a better relative sensitivity is obtained by adding lauryl pyrimidium chloride into a pretreatment solution (2.8 or 3.475) than into an assay solution (2.60).

The results observed in the present invention are, therefore, superior to those observed in US 09/269897, when comparing the closest possible data. This superiority is not disclosed in the prior art, predicted by the prior art, or explained by any theory, and is perforce an unexpected result. Because the presently claimed invention exhibits unexpected results, the claims are not obvious. Reconsideration and withdrawal are respectfully sought.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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TABLE A

			Present Invention					US 09/269897						
		Conc. (%)	#110	#120	#117	#89	#89' (-0.2)	#45	#46	#3	#7	#19	Average	Corrected Average
	Cationic surfactant	0	0.031	0.128	0.123	0.322	0.122	15.67	1	1.15	1.34	1.19		
C12	Dodecyl pyridinium chloride	0.5	0.069	0.305	0.598	0.542	0.542							
	0.5%/0% S/N ratio		2.2	2.4	4.9	1.7	4.4						**2.80**	**3.475**
	Dodecyl pyridinium chloride	0.5						53.43	4.7	2.05	1.52	2.33		
	0.5%/0% S/N ratio							3.4	4.7	1.8	1.1	20.	**2.60**	
C10	Decyltimethylammonium chloride	0.5	0.074	0.303	0.449	0.686	0.686							
	0.5%/0% S/N ratio		2.4	2.4	3.7	2.1	5.6						**2.65**	**3.525**
	Decyltrimethylammonium chloride	0.5						17.5		0.88	0.8	0.72		
	0.5%/0% S/N ratio							1.1		0.8	0.6	0.6	**0.775**	